Amendments to the Specification:

Please amend the specification in the following manner:

Please replace the heading and the paragraph beginning at line 10 of page 1, with the following new heading and amended paragraph:

CROSS-REFERENCES TO RELATED APPLICATIONS/GOVERNMENT RIGHTS

This application is a continuation of U.S. Patent Application No. 09/534,706, filed March 23, 2000, now abandoned, which is a continuation-in-part of U.S. Patent Application No. 09/018,226, now U.S. Patent No. 6,150,416, issued November 21, 2000, and claims the benefit of these applications, U.S. Provisional Application No. 60/125,958, filed March 24, 1999, and U.S. Provisional Application No. 60/036,903, filed February 4, 1997, the disclosures of which are incorporated by reference. This invention was made with Government support under Grant (Contract) Nos. RO1 GM53696 and RO1 GM50353 awarded by the National Institutes of Health. The Government has certain rights in this invention.

Please replace the paragraph beginning at line 1 of page 10 with the following amended paragraph:

FIGS. 15A and 15B illustrate the time course and dose dependency for suppression of phosphorylated tau fragments by a cathepsin D inhibitor. (A). Cultured hippocampal slices were incubated for 2, 4, or 6 days with the cathepsin B/L inhibitor-ZPAD, the cathepsin D inhibitor-EA-1, or both. Western blot analyses for phosphorylated tau fragments were carried out at the end of the incubation with densitometric values expressed as percent of concentrations in yoked controls. ZPAD induced increases were detectable after 48 hrs and continued to grow thereafter. The cathepsin D inhibitor had no apparent effect but blocked the increases produced by ZPAD at all time points. (B). Slices were incubated with ZPAD, EA-1, or ZPAD plus the indicated concentrations of EA-1 for six days. The cathepsin D inhibitor had no detectable effects on concentrations of phosphorylated tau fragments at the concentrations tested.

A dose of 1 μM caused a sizeable decrease in the effect of ZPAD while 5 μM completely suppressed it. *, $P<0.05$; **, $P< 0.01$; error bars, standard errors.

Please replace the paragraph beginning at line 14 of page 10 with the following amended paragraph:

FIGS. 16A and 16B illustrate the effects of cathepsin inhibitors on tau and cathepsin D isoforms. Slices were incubated with ZPAD, EA-1, or both for 6 days after which Western blots were used to assess the concentrations of the target proteins with tau 1 antibodies (A), or anti-cathepsin D antisera (B). Densitometeic values were expressed as percent change from the concentrations in yoked control slices. (A). ZPAD caused sizeable reductions in four unphosphorylated isoforms of native tau; EA-1 was without effect itself and did not block the changes produced by ZPAD. ZPAD also generated a large increase in a 29 kDa tau fragment; this was completely blocked by EA-1. (B). ZPAD resulted in modest increases in procathepsin D and larger increases in the active, heavy chain variant of the protease. EA-1 suppressed the second of these effects.